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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/554,424	11/06/95	VAN DER PLOEG L	19338DA

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EXAMINER	
LUBET,M	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/554,424	Applicant(s) Van Der Ploeg et al.
	Examiner Lubet	Group Art Unit 1644

☒ Responsive to communication(s) filed on *4/28/98 and 6/29/98*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *20-26* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *20-26* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Group 1600 Art Unit 1644.

2. The request in Paper 11 filed on April 28, 1998 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/554,424 is granted. This office action is in response to Paper 11 filed April 28, 1998 and Paper 12 filed July 14, 1998.

3. Claims 20-26 are under examination. Examiner acknowledges amendment to claim 20 in Paper 12.

4. (maintained) Claims 20-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. (maintained)In claim 20, it is unclear if the cell in which para and tipE are expressed lacks a voltage-activated sodium channel prior to the induction of expression of para and tipE gene products. If so, what cells lack a voltage-activated sodium channel?

--Applicant's response on page 3 of Paper 12 has been considered but is not persuasive. Applicant's argument that the amended claimed language recites a method wherein the difference in absolute voltage induced is compared in a cell prior to and after induction of expression of para and tipE is not persuasive since the claimed method of identifying ligands that modulate Drosophila membrane sodium channel does not recite a limitation wherein the difference in voltage induced in a cell prior to and after expression of para and tipE gene products is measured.

The claimed methods pertain to comparing differences in voltage induced between cells expressing recombinant para and tipE with the voltage induced in control cells not expressing (cells in which RNA or cDNA encoding para and tipE have not been introduced).

Applicant's response that cells which lack voltage activated sodium channels prior to the induction of par and tipE gene products are well known in the art by pointing out specific places in the specification which disclose that COS-1, CV-1 and 293 L cells may used as host cells for vectors comprising DNA encoding para and tipE is not persuasive. There is no evidence of record to show that these cells lack voltage activated channels.

Applicant may want to address this issue by amending the claims to recite a limitation wherein the sodium channel is tetrodotoxin sensitive.

B. (Withdrawn) In claim 22, it is unclear what the term "are introduced into the host cell" means. Does this term encompass injection of isolated DNA molecules encoding para and tipE genes into the cells and transfection of vectors which comprise para and tipE genes? If the claim language encompasses transfection of vectors which comprise para and tipE genes, must the para and tipE genes be in the same vector or does the claim language encompass co-transfection with two vectors, one comprising para gene and the other the tipE gene?

--Applicant's response on pages 4-5 of Paper 12 has been considered and is persuasive. Applicant's response indicates that the claim language should be interpreted broadly and that the specification supports introducing the of DNA encoding para and tipE genes on the same vector

or by introducing two DNA molecules, one encoding para gene product and one encoding the tipE gene product.

C. Claim 20 contains a typographical error. On line 4 of claim 20 a period follows the word "tipE". Correction is required.

5. **New rejection of claims under 35 USC 112, first paragraph necessitated by amendment.**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. The method of identifying ligands that modulate Drosophila membrane sodium channel by comparing the voltage-activated current measured in a cells co-expressing Drosophila para voltage channel and an isolated tipE claimed in Claims 20-26 has no clear support in the specification and the claims as originally filed. The specification discloses methods of identifying ligands that modulate voltage activated sodium channel by determining tetrodotoxin sensitive modulation of radioactive sodium uptake or modulation of tetrodotoxin induced cellular toxicity. However, there is no support for the claimed method of identifying ligands that modulate Drosophila membrane sodium channel by measuring the ability of the ligand to modulate voltage-activated current.

The specification discloses a method of identifying ligands that modulate a Drosophila membrane sodium channel in para transfected cells but does not disclose a method in which the cells co-expresses an Drosophila para voltage activated sodium channel and a beta subunit of tipE.

The subject matter claimed in claims 20-26 broadens the scope of the invention as originally disclosed in the specification. If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification by pointing to specific pages and lines in the originally filed specification.

Applicant may want to address this issue by amending the claims to recite a limitation wherein the sodium channel is tetrodotoxin sensitive.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. **(maintained)** Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jackson et al (D)(J. of Neurogenetics 3: 1, 1986) in view of O'Dowd et al (J)(J. Of Neuroscience 8:3633, 1988).

A. Jackson et al. teach double Drosophila mutants expressing $para^{ts-1}$ and tipE (see pages 10-11, in particular). Thus cells isolated from these double mutants express para and tipE and are from a multicellular organism. Jackson et al. does not disclose a method of identifying ligands that modulate Drosophila membrane sodium channels. However, O'Dowd et al. teach a method of identifying ligands that modulate sodium channel in Drosophila neurons of tipE mutant Drosophila *in vitro* by measuring the ability of ligands such as tetrodotoxin to modulate the voltage-activated current (see Figure 6 and pages 3637, in particular). Therefore it would have been *prima facie* obvious to one with skill at the time of the invention to substitute cells from the para/tipE double mutant taught by Jackson et al. for the tipE mutant cells used in the assay taught by O'Dowd et al. with the expectation that the assay would identify ligands that modulate the Drosophila membrane sodium channel.

--Applicant's response on page 5-6 of Paper 12 have been considered but are not persuasive. Applicant's argument that amended claim 20 is directed to host cells in which isolated tipE and para genes have been introduced as isolated genes for co-expression is not persuasive because claim 20 does not recite a limitation that the host cell expressing para and tipE must be cells in which the tipE and para genes have been introduced as isolated genes for co-expression. The claim language reads upon any cell from a multicellular organism which coexpresses para and tipE, including cells isolated from double mutants expressing para and tipE. The use of the term "isolated" in claim 20 does not help to limit the claim to cells in which tipE and para genes have introduced.

Applicant may wish to address this rejection by amending the claims to claim a method of identifying ligands that modulate a Drosophila membrane sodium channel which comprises introducing into a host an isolated nucleic acid encoding a Drosophila voltage activated para alpha subunit and an isolated nucleic acid encoding a Drosophila voltage activated tipE beta subunit under conditions sufficient to co-express the gene products of para and tipE.

8. (withdrawn) The rejection of Claims 20-23 under 35 U.S.C. 103(a) as being unpatentable over MacKinnon et al. (UU)(Neuron 5, 767, 1990) in view of Jackson et al.(D) and further in view of Loughney et al. (M)(Cell 58: 1143, 1989) and Hall et al. (H)(in Drosophila, 35th Annual Drosophila Res. Conference vol. 77, April, 1994) is withdrawn.

--Applicant's response of pages 6-7 has been carefully considered and is persuasive. Applicant's argument that Hall et al. is not an enabling disclosure for an isolated tipE gene is persuasive.

NEW REJECTION under 35 USC 103(a)

9. Claims 20-23 are rejected under 35 U.S.C. 103(a) as being anticipated by Hall et al. US 5,593,862 (issued Jan. 14, 1997, filed Oct. 4, 1994).

A. The '862 patent discloses co-expressing isolated DNA molecules encoding Drosophila para and isolated DNA molecule encoding TipE in a host cell (see claims 23 and 24, in particular). The '862 patent also discloses coexpressing Drosophila para and tipE by introducing into Xenopus oocytes tipE mRNA and para mRNA (see column 9, line 14 though column 10, line 23, and column 25, line 45 through column 26, line 19, in particular). The '862 patent also teaches a method of identifying ligands that modulate Drosophila membrane sodium channel by

contacting the host cell expressing isolated para and tipE with a ligand and measuring the resulting voltage-activated current (see column 26, lines 1-19, in particular). The '892 Patent discloses a method for identifying modulators of Drosophila sodium channel by transforming cells with isolated gene encoding tipE and isolated gene encoding para and screening agents which modulate voltage dependent cation channel activity of such a cell by measuring cation current (see column 10, lines 31-65, in particular). *Xenopus* oocytes are host cells from a multicellular organism.

Therefore one with skill in the art would be motivated to identify ligands that modulate Drosophila membrane sodium channel using the techniques taught by the '892 patent by coexpressing isolated DNA molecules encoding para and DNA encoding tipE in host cells such as Xenopus oocytes and determining if the ligand modulates the voltage activated current in the transformed cells as compared to control cells not transformed with the DNA encoding para and tipE gene products. One with skill in the art would be motivated to modify the screening methods taught by the '862 Patent by substituting cells coexpressing Drosophila para and tipE by introducing into *Xenopus* oocytes tipE mRNA and para mRNA for the cells transformed with DNA encoding para and tipE gene products using the methods disclosed by the '892 patent with the expectation that such a method would identify modulators of Drosophila membrane sodium channel.

10. A prior art search of the embl-new3, EST-STS and geneseq27 data bases does not reveal a DNA with the exact sequence as SEQ ID. NO. 7. However, SEQ ID NO. 7 differs from the para

sequence taught by Loughney et al. only in residues 3613-3815 which correspond to residues 3367-3612 of SEQ ID. No. 7. Therefore claims 24-26 are free of the prior art.

11. Examiner believes that all pertinent arguments have been addressed.

12. No claim is allowed. THIS ACTION IS NON- FINAL.

132. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Martha Lubet in Art Unit 1644 whose telephone number is (703) 305-7148. The examiner can normally be reached on Monday through Friday from 8:15 AM to 4:45 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (703) 305-3973 The FAX number for this group is (703) 305-3014 or 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Martha T. Lubet

Sept. 16, 1998

THOMAS M. CUNNINGHAM
PRIMARY EXAMINER
GROUP 1800